

## PATENT COOPERATION TREATY


## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

|  |   |   |
|--|---|---|
| Applicant's or agent's file reference<br>ISPH-0377   | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |   |
| International application No.<br>PCT/US99/16219  | International filing date (day/month/year)<br>19 JULY 1999  | Priority date (day/month/year)<br>25 SEPTEMBER 1998 |
| International Patent Classification (IPC) or national classification and IPC<br>Please See Supplemental Sheet. |   |   |
| Applicant<br>ISIS PHARMACEUTICALS, INC.  |   |   |

|   |
|---|
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>24</u> sheets.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p>  |
| <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step or industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p> |

|  |   |
|--|---|
| Date of submission of the demand<br>18 APRIL 2000  | Date of completion of this report<br>20 JULY 2000   |
| Name and mailing address of the IPEA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231 | Authorized officer<br>ANDREW WANG  |
| Facsimile No. (703) 305-3230   | Telephone No. (703) 308-1235  |

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/16219**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : CO7H 21/04; A61K 48/00; C12Q 1/68; C12N 15/85

US CL : 435/6, 325, 366; 514/44; 536/23.1, 24.5

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 325, 366; 514/44; 536/23.1, 24.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, MEDLINE, EMBASE, SCISEARCH, CAPLUS, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|-----------|---|-----------------------|
| A         | GEWIRTZ et al. Facilitating oligonucleotide delivery: Helping antisense deliver on its promise. Proc. Natl. Acad. Sci. April 1996, Vol. 93, pages 3161-3163, see entire document. | 1-18                  |
| A         | BRANCH. A good antisense molecule is hard to find. TIBS. February 1998. Vol. 23, pages 45-50, see entire document   | 1-18                  |

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

|   |  |
|---|--|
| Special categories of cited documents:  |  |
| "A" document defining the general state of the art which is not considered to be of particular relevance  | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| "E" earlier document published on or after the international filing date  | "X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "O" document referring to an oral disclosure, use, exhibition or other means  | "&" document member of the same patent family  |
| "P" document published prior to the international filing date but later than the priority date claimed  |  |

Date of the actual completion of the international search

10 SEPTEMBER 1999

Date of mailing of the international search report

29 NOV 1999

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
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**I. Basis of the report****1. With regard to the elements of the international application:\***☒ the international application as originally filed☒ the description:

pages 1-53 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of

☒ the claims:

pages 54-55 , as originally filed  
pages NONE , as amended (together with any statement) under Article 19  
pages NONE , filed with the demand  
pages NONE , filed with the letter of

☒ the drawings:

pages NONE , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of

☒ the sequence listing part of the description:

pages 1-11 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**☒ contained in the international application in printed form.☒ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.**4. ☒ The amendments have resulted in the cancellation of:**☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets/fig. NONE**5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

|                               |                    |     |
|-------------------------------|--------------------|-----|
| Novelty (N)                   | Claims <u>1-18</u> | YES |
|                               | Claims <u>NONE</u> | NO  |
| Inventive Step (IS)           | Claims <u>1-18</u> | YES |
|                               | Claims <u>NONE</u> | NO  |
| Industrial Applicability (IA) | Claims <u>1-18</u> | YES |
|                               | Claims <u>NONE</u> | NO  |

**2. citations and explanations (Rule 70.7)**

Claims 1-18 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claimed antisense oligos which specifically inhibits RhoG expression nor methods inhibiting RhoG or treatment using said antisense oligos.

Claims 1-18 meet the criteria set out in PCT Article 33(4), for industrial applicability.

----- NEW CITATIONS -----  
NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/16219

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): C07H 21/04; A61K 48/00; C12Q 1/68; C12N 15/85 and US Cl.: 435/6, 325, 366; 514/44; 536/23.1, 24.5